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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
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EXAMINER	
MARTIN, J	
ART UNIT	**PAPER NUMBER**
1632	12

DATE MAILED: 06/21/00

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

FILE

Office Action Summary

Application No.	Applicant(s)
09/096,648	Hadlaczky & Szalay
Examiner	**Group Art Unit**
Jill D. Martin	1632

☒ Responsive to communication(s) filed on *Mar 31, 2000* .

☒ This action is **FINAL.**

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire *3* month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☒ Claim(s) *32-44, 59, 60, and 64-81* is/are pending in the application.

Of the above, claim(s) _____ is/are withdrawn from consideration.

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) *32-44, 59, 60, and 64-81* is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐approved ☐disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____ .

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____ .

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☐ Notice of References Cited, PTO-892

☐ Information Disclosure Statement(s), PTO-1449, Paper No(s). _____

☐ Interview Summary, PTO-413

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

Applicants' Amendment filed February 22, 2000 (Paper No. 10) has been entered. Claims 1-31, 45-58, and 61-63 have been canceled, claims 32, 35-44, 59, and 60 have been amended, and claims 64-81 have been added. Applicants' Supplemental Response filed March 31, 2000 (Paper No. 11) has been entered. The Perez Declaration under 1.132 filed March 31, 2000 (Paper No. 11) has been considered as indicated below. Claims 32-44, 59, 60, and 64-81 are pending and are under current examination.

Rejections made of record in the prior Office action (Paper No. 6) not made of record in the instant Office action have been withdrawn in view of Applicants' arguments, amendments to the claims, and/or the Perez Declaration under 1.132.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The Perez Declaration under 1.132 is sufficient to reduce the issues under 35 U.S.C. §112, first paragraph as follows:

Claims 32-41, 43, 44, 59, 60, 64-67, and 71-74 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for methods for making a transgenic mouse using SATACs comprising at least one heterologous gene such that the heterologous gene is expressed at detectable levels, and wherein the method comprises specific steps leading to the

production of the transgenic mouse, does not reasonably provide enablement for the claimed methods of producing transgenic animals of **any and all** species, **wherein the method recites only that an embryonic cell is exposed to conditions to produce the transgenic animal, and wherein the expression of the heterologous gene leads to an immunoprotective effect**. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

Claims 32-41, 43, 44, 59, 60, 64-67, and 71-74 are directed to the methods of making transgenic animals using SATACs.

Applicants' arguments and evidence provided in the Perez Declaration under 1.132 are persuasive to enable methods of using SATACs to produce transgenic mice expressing heterologous genes at detectable levels, in so far as the method includes steps fully describing the generation the mice. However, the evidence of record pertaining to the production of transgenic mice fails to provide a nexus towards the production of transgenic animals of species other than mice. Applicants argue that the level of skill and the state of the art was such that transgenic animals other than could have been generated based on the teachings present in the specification. See pages 10-15 of the Amendment (Paper No. 10). In response, it is noted that the specification only refers to transgenic methodology pertaining to the production of transgenic mice, in particular such methodology does not include the use of SATACs or other MACs. See pages 108, 110, and 111 of the specification. Furthermore, pages 13-14 of the prior Office action

(Paper No. 9) cite references of record which support that transgene behavior in mice cannot be extrapolated to other species of animals, in particular, as the instant claims pertain to the use of SATACs, the state of the art is undeveloped for transgenics and thus, would not be any different from extrapolation of a transgene from one animal to another than from a SATAC comprising a transgene from one animal to another. Evidence providing a nexus between a transgenic mouse and other transgenic animals by use of SATACs is necessary to enable the breadth of the claimed methods.

Applicants argue that the amount of guidance and direction is sufficient for the claimed invention. See pages 16-18 of the Amendment (Paper No. 10). Applicants' argument is considered, and partially persuasive for such guidance to be extended to the production of transgenic mice as supported by the Perez Declaration under 1.132. The Perez Declaration teach the production of transgenic mice whose genome comprises a SATAC comprising heterologous DNA. The expression of such DNA, β-gal and hph, is demonstrated to be detectable. However, such evidence cannot be extrapolated to expression of such DNA in other animals nor expression of such DNA to cause a immunoprotective phenotype in any animal including in mice. Note that the Perez Declaration is silent regarding the expression of the anti-HIV gag ribozyme, particularly with regard to expression levels sufficient to convey immunoprotection.

With regard to the introduction of MACs into ES cells, Applicants argue that methods for developing transgenic animals through initial introduction of transgenes into embryonic stem cells are known in the art regardless of the number of species of embryonic stem cells that may exist.

Applicants go on to argue that the cited references of record does not appear to fairly support the Examiner's statement that only mouse ES cells were available for the use of transgenics. Here, Applicants refer to Mullins et al. and Seamark. See pages 35-36 of the Amendment (Paper No. 10). In response, however, it is maintained that the cited references of record clearly support the Examiner's statement because it is maintained that the art- recognized definition of an embryonic stem (ES) cell is one that contributes to the germline as well as the whole animal. Moreadith et al. on page 209, column two, for example, supports this observation as they discuss the historical perspective of mouse ES cells as follows:

"The stage was set-one could grow normal, diploid ES cells in culture for multiple passages without loss of the ability to contribute to normal development. Furthermore, the cells contributed to the development of gametes at a high frequency (germline competence), and the haploid genomes of these cells were transmitted to the next generation. Thus, the introduction of mutations in these cells offered the possibility of producing mice with a predetermined genotype."

As such, it is maintained that Mullins et al. & Seamark support that in no species other than the mouse has germline transmission of an ES cell been demonstrated, and an isolated ES cell from a pig, for example, which has not been demonstrated to contribute to the germline of the animal does little towards the production of transgenic animals of species other than the mouse. Therefore, it is maintained that the method claims so limited to the use of embryonic cells, should also be limited to the use of mouse embryonic stem cells as these are the only embryonic stem cells which have been shown to give rise to germline tissues and the whole animal.

Note that claim 42, and new claims 68-70, and 75-81 stand rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention, for the reasons of record advanced on pages 6-16, particularly pages, 6, 8, 14, and 15, for example.

Claims 42, 68-70, and 75-81 are directed to products produced by the methods above, namely, the transgenic animals or mice comprising SATACs.

The enablement standard requires that the specification teach both how to make and how to use the claimed invention. As such, although the Perez Declaration supports the production of transgenic mice using SATACs and confirms the expression of detectable marker genes, it fails to teach how to use these mice as expression fails to convey a useful phenotype as a result of expression. The specification specifically discusses that their method of using SATACs provides a means for producing a disease-resistant transgenic animal. See page 40, lines 14-16. However, the specification as well as the evidence presented in the Perez Declaration fail to support that expression of any gene would result in immunoprotection. It is noted that with regard to claim breadth, the standard under 112, first paragraph entails the determination of what the claims recite and what the claims mean as a whole. In addition, when analyzing the enabled scope of the claims, the teachings of the specification are taken into account because the claims are to be given their broadest reasonable interpretation that is consistent with the specification. As such, in light of the specification, the claimed invention is properly interpreted with regard to the disclosed use

of the claimed transgenic animals comprising SATACs for conveying a state of disease-resistance. Such an interpretation is consistent with the specification despite that the claimed non-human animals require only that they comprise SATACs. As such, it is maintained that the specification fails to enable the claimed transgenic non-human mammals, including the claimed transgenic mice.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 32-44, 59, 60, 64-78 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

It is maintained that claims 32-41, 43, 44, 59, 60, 64-67, and 71-74 are incomplete as written. The claim amendments do not overcome the rejection of record as the claims are now drawn to "exposing an animal cell containing the SATAC to conditions whereby a transgenic animal develops therefrom." It is still a huge leap to go from exposing a cell to conditions and the production of a transgenic animal, and it is not clear how mere exposure of a cell to certain unspecified conditions would be sufficient to produce a transgenic animal. More is required, including essential steps such as, introducing an embryonic stem cell or fertilized ovum

(comprising the SATAC) into an embryo, transplanting the embryo into a recipient non-human animal, allowing the embryo to develop to term, identifying a transgenic non-human animal whose genome comprises the SATAC (comprising the heterologous DNA).

Conclusion

Claims 32-44, 59, 60, and 64-81 appear to be free of the prior art of record for the reasons of record advanced on page 23 of the prior Office action mailed 8/17/99 (Paper No. 9), however, these claims are subject to other rejections.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jill Martin whose telephone number is (703)305-2147.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jasemine C. Chambers, can be reached at (703)308-2035.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703)308-0196.

Papers related to this application may be submitted by facsimile transmission. Papers should be faxed via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center numbers are (703)308-4242 and (703)305-3014.

Jill D. Martin

Patent Examiner

Jasemine C. Chambers

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